Routine Offering of HIV Testing to Hospitalized Pediatric Patients at University Teaching Hospital, Lusaka, Zambia: Acceptability and Feasibility

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Objectives: The difficulties diagnosing infants and children with HIV infection have been cited as barriers to increasing the number of children receiving antiretroviral therapy worldwide.

Design: We implemented routine HIV antibody counseling and testing for pediatric patients hospitalized at the University Teaching Hospital, a national reference center, in Lusaka, Zambia. We also introduced HIV DNA polymerase chain reaction (PCR) testing for early infant diagnosis.

Methods: Caregivers/parents of children admitted to the hospital wards were routinely offered HIV counseling and testing for their children. HIV antibody positive (HIV+) children <18 months of age were tested with PCR for HIV DNA.

Results: From January 1, 2006, to June 30, 2007, among 15,670 children with unknown HIV status, 13,239 (84.5%) received counseling and 11,571 (87.4%) of those counseled were tested. Overall, 3373 (29.2%) of those tested were seropositive. Seropositivity was associated with younger age: 69.6% of those testing HIV antibody positive were <18 months of age. The proportion of counseled children who were tested increased each quarter from 76.0% in January to March 2006 to 88.2% in April to June 2007 ($P < 0.001$). From April 2006 to June 2007, 1276 PCR tests were done; 806 (63.2%) were positive. The rate of PCR positivity increased with age from 22% in children <6 weeks of age to 61% at 3–6 months and to 85% at 12–18 months ($P < 0.001$).

Conclusions: Routine counseling and antibody testing of pediatric inpatients can identify large numbers of HIV-seropositive children in high prevalence settings. The high rate of HIV infection in hospitalized infants and young children also underscores the urgent need for early infant diagnostic capacity in high prevalence settings.

Key Words: Africa, early infant diagnosis, HIV testing, pediatric HIV, provider initiated testing and counseling

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INTRODUCTION

Recent efforts to provide antiretroviral therapy (ART) to HIV-infected individuals in resource-limited countries have met with considerable success.[1] More than 2.1 million individuals in sub-Saharan Africa were reported to have initiated ART by December 2007.[1] These successes have been predominantly limited to adults: efforts to treat HIV-infected children have been less robust. By the end of 2007, an estimated 2.5 million children worldwide were living with HIV, but only 200,000 children were receiving ART.[1,2]

Multiple barriers to pediatric ART have been delineated.[3–7] Pediatric formulations are more costly than adult medications and require precise dosing based on weight or body surface area.[8] Pediatric fixed-dose combination tablets only recently became available.[9,10] Pediatric expertise is often limited, with few health care providers trained to care for children with complex conditions. And, in the context of large numbers of adults with HIV, few governments have prioritized the needs of children.

Identifying and diagnosing HIV-infected children have also posed formidable barriers to engaging children in care. Prevention of mother-to-child transmission (PMTCT) programs offer opportunities to identify HIV-exposed infants, but the scale-up of PMTCT programs has been eclipsed by efforts to roll-out ART, and routine infant follow-up has been difficult to achieve.[11,12] Furthermore, until recently, there has been limited guidance on pediatric HIV testing policies and a reliance on risk-based offering of testing.[13] The rapid rate of pediatric disease progression and overlap of symptoms with other diseases have shown this approach to be inadequate to prevent HIV-related mortality.[14–19] Finally, the complexity of

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diagnosing HIV infection in infants and young children often precludes early ART initiation.[20–25] Special virologic tests such as RNA or DNA polymerase chain reaction (PCR) are required to determine if an HIV-exposed infant is infected.[20–25]

In Zambia, with the rapid scale-up of HIV services, 11,602 children were receiving ART at the end of 2007.[12] At the University Teaching Hospital of Zambia (UTH), the national reference hospital in Lusaka Zambia, there are more than 10,000 pediatric admissions annually. Because HIV-exposed and HIV-infected children are at high risk for infectious and nutritional complications, we hypothesized that routinely offering HIV antibody testing to all hospitalized children would identify large numbers of HIV-positive children.[26,27] In January 2006, we initiated a program to routinely offer counseling and HIV antibody testing with same day results for all children hospitalized at UTH. We present the results for the first 18 months of activity and results of an early infant diagnosis (EID) program using DNA PCR initiated in May 2006.

METHODS

Pediatric Center of Excellence at UTH in Lusaka, Zambia

The Republic of Zambia is a large landlocked country in subequatorial Africa with an estimated 11.5 million inhabitants. The per capita income is US $395 placing Zambia amongst the poorest nations in the world. The HIV seroprevalence in urban antenatal clinics is approximately 25%, and it is estimated that 28,000 infants are born with HIV infection annually.[12,28] In collaboration with international partners, the Zambian government began to scale-up HIV services in April 2004 and in August 2005 began to provide free ART for adults and children.[28–30]

The Pediatric Center of Excellence (PCOE) was established at UTH to provide comprehensive care for HIV-exposed and HIV-infected children and training and dissemination of pediatric HIV expertise. The PCOE is part of the UTH Department of Pediatrics and Child Health and is supported through a collaborative relationship with the Zambian Ministry of Health, the US Centers for Disease Control and Prevention with funding through the President's Emergency Plan for AIDS Relief, and the International Center for AIDS Care and Treatment Programs, Columbia University Mailman School of Public Health. The PCOE has fostered a relationship between UTH, Boston University, and Columbia University to support pediatric HIV care.

UTH serves as the tertiary referral center for urban and peri-urban communities in Lusaka. There are 450 pediatric inpatient beds and 1 admission ward, 3 general wards, specialty wards for malnutrition, isolation, diarrhea/rehydration, and fee-paying patients, and neonatal and pediatric intensive care units. Most children requiring hospitalization remain on the admission ward during the first 24 hours after which they are admitted to an inpatient ward.

Development of the Pediatric Inpatient HIV Testing Program

Before the initiation of the program, hospitalized children were referred to the family support unit (FSU), a freestanding voluntary counseling and testing site on the hospital campus. Patients had to be ambulatory to reach the FSU. On occasion, FSU counselors tested children on the wards. The FSU was staffed by 3 counselors and 7 volunteers who could draw blood from children and perform HIV rapid antibody tests. Over the 2-year period, 2004–2005, of approximately 20,000 children admitted to UTH, 1276 children had HIV testing at the FSU.

In September 2005, the inpatient testing program was piloted. Two FSU counselors were deployed to the admission ward to provide individual counseling to parents and caregivers. If the family refused testing, was unavailable, or the child was considered medically unstable, the caregiver was approached later during the hospitalization. Patients admitted at night, on weekends, or holidays when counselors were unavailable were approached at the earliest opportunity.

Counselors obtained a venous blood sample and ran HIV antibody testing once verbal permission was granted. The tests were performed in a renovated room within the admissions ward using the Abbott Determine rapid test kit. Positives were confirmed with Genie II. All children testing HIV positive were offered enrollment in care at the PCOE or at the local district clinic.[29] Clinical and immunological staging was initiated during the hospitalization, and cotrimoxazole was prescribed.

The introduction of counselors to the wards was facilitated by a series of sensitization workshops with hospital staff. The workshops focused on engaging all staff to recognize and deliver the message of the importance of HIV testing in the routine care and hospital management of pediatric patients. Staffs were also engaged in assuring that a work-up was completed and that all HIV-positive children were offered follow-up care.

In January 2006, after 3 months of piloting, the program was fully instituted. Two additional counselors were hired to provide services for all patients admitted to the admissions ward during weekday working hours and to children on other wards who had not been tested. With time, there was a shift from individualized to group pretest counseling. Furthermore, parents of children testing HIV positive were offered HIV testing and, if positive, were referred for HIV treatment services.

In January of 2006, with support from the US Centers for Disease Control and Prevention, HIV DNA PCR became available for EID at the UTH laboratory. After piloting the methodology, in May 2006, EID testing became routinely available for hospitalized children <18 months of age using whole blood samples. An HIV proviral DNA–based commercial assay (Roche Amplicor 1.5) was used.[31,32] For quality assurance, a simplified, real-time, duplex, reverse transcription PCR assay was employed.[22]

Data Collection

Counselors recorded patient's date of birth, sex, date of counseling, testing, HIV test results, and reason, if child was not tested, in a logbook located on each ward. Data from logbooks were entered into an electronic database. Documented reasons for not testing were categorized during data analysis. Beginning in August 2006, when the parent/caregiver

showed documentation of prior HIV testing, reason for not testing was coded as "documented known status." The accuracy of the logbooks was reviewed weekly by comparing them with nurses' summary reports.

All samples for EID testing were recorded in a specimen logbook. Laboratory staff maintained a separate electronic database of test results, which included a unique patient number, age, sex, ward, and collection date.

Statistical Methods

Demographic characteristics of children ≤15 years of age are described, and counseling and testing rates were calculated for each hospital ward. Only children whose families received counseling were included in analyses of HIV testing. We evaluated the relationship between child's sex, age, and ward on seropositive status and the proportion of children counseled and tested using Mantel–Haenzel Chi square tests of association and Wilcoxon rank sum tests, excluding missing values, and logistic regression for multivariate modeling. Changes in counseling and testing coverage from the start of the program to most recent calendar quarter were evaluated using χ^2 tests. Differences in seroprevalence based on DNA PCR testing were evaluated by age, gender, and calendar quarter. To estimate the proportion of eligible children who received DNA PCR testing, we compared the number of DNA PCR tests performed each quarter with the number of children <18 months of age who tested HIV antibody positive during the same period. Data analysis was performed using SPSS 14.0 (SPSS Inc., Chicago, IL).

RESULTS

From January 1, 2006, through June 30, 2007, there were 21,000 admissions to UTH, including 3997 (19.5%) repeat admissions for 17,003 children. Pediatric patients had a median age of 12 months (interquartile range: 0–24 months); 62.6% were younger than 18 months, and 52.6% were male. More children were admitted monthly during the rainy season when hospitalization rates increased secondary to diarrhea diseases (quarter 4, October to December 2006, and quarter 5, January to March 2007).

The parents/caregivers of 1333 (6.7%) children reported that their child's HIV status was already known: 765 (57.4%) HIV antibody positive; 368 (27.6%) HIV antibody negative; and 200 (15.0%) HIV status not recorded. These children were excluded from further analysis.

Among the remaining 15,670 children with unknown HIV status 13,239 (84.5%) received counseling and 11,571 (87.4%) counseled children were tested (Table 1). Age and hospital ward were significantly associated with counseling, testing, and seropositive status. The highest counseling rates were found among children <12 months of age (86.4%) and among admissions to the malnutrition (88.4%) and diarrhea/rehydration (91.5%) wards. Testing rates showed a similar pattern.

Overall, 3373 children, 29.2% of those tested, were HIV antibody positive with the highest rates among children <6 months of age (32.4%) and the lowest rates among children >5 years (23.4%); 69.6% of all children testing HIV antibody positive were <18 months of age (Table 1). Females had a slightly higher seropositivity rate than males (31.3% vs. 27.0%; $P = 0.013$), however, counseling and testing rates were not associated with gender. Seropositive status was also associated with inpatient ward with the highest rate (36.6%) found among children admitted to the malnutrition ward. After adjusting for age, sex, and calendar quarter, children in the malnutrition (adjusted odds ratio: 16.7; 95% confidence interval: 13.7 to 20.4) and diarrhea/rehydration wards (adjusted odds ratio: 8.2; 95% confidence interval: 6.6 to 10.2) were significantly more likely to test seropositive than children in general pediatric wards.

As shown in Figure 1, the proportion of children counseled and tested increased from the beginning of the program to the last quarter: 79.9% and 76.0% in quarter 1, January to March 2006, to 88.2% and 87.4% in quarter 6, April to June 2007, ($P < 0.001$), respectively. Seropositivity rates decreased over time from 35% during quarter 1 to 23% during the last quarter of testing ($P < 0.001$).

Of the 4099 eligible children who did not receive HIV antibody testing, 2431 (59.3%) received neither counseling nor testing, and 1668 (40.6%) were counseled but not tested. Reasons for not testing were recorded for 2111 (52.0%) children (Table 2). The most common reasons for not testing were child died (43.6%), parent refused (12.0%), and discharged early (9.6%). Many of the categories represent missed testing opportunities: early discharge, absconded, and weekend admission. The majority of children in these categories received no counseling. In contrast, parental refusal and waiting for husband's permission represent situations where counseling was performed, but the child was not tested.

EID Using DNA PCR

A total of 1276 hospitalized children <18 months of age had PCR tests between May 2006 and June 2007: 806 (63.2%) tested DNA PCR positive, 453 (35.5%) negative, 2 (0.5%) indeterminate, and 15 (1.3%) unavailable results. The proportion of eligible children who were tested increased from 44% when testing became available to 70% during the most recent quarter, quarter 6, April to June 2007. Older age was strongly associated with PCR positivity: more than 85% of 186 children between 12 and 18 months of age tested positive, whereas only 22% of 140 children <6 weeks of age were positive ($P < 0.01$) (Fig. 2).

DISCUSSION

This is the first report of the implementation of a routine HIV antibody testing program for hospitalized pediatric patients in a high HIV prevalence, low-resource setting. At the UTH in Lusaka, Zambia, over 18 months, 13,239 parents/caretakers received counseling for HIV antibody testing of their hospitalized child, representing 84.5% of children with unknown HIV status. Overall, more than 11,000 children were tested, and during the last quarter of the program, 87% of those counseled had antibody testing. Approximately, 30% of those tested HIV antibody positive reflecting the high rates of morbidity seen in HIV-exposed and HIV-infected children and the significant contribution of HIV to the disease burden on pediatric hospital wards.[14,18,19,33–36]

TABLE 1. Demographic and Baseline Characteristics of Children Admitted to UTH, January 2006 to June 2007 (N = 17,003)

	TOTAL		Counseled (n = 15,670)					Tested (n = 13,239)					Test Result (n = 11,571)				
	N	%	Yes	%	No	%	*P*	Yes	%	No	%	*P*	Negative	%	Positive	%	*P*
Total*	17,003	100	13,239	84.5	2431	15.6	—	11,571	87.4	1668	12.6	—	8198	70.8	3373	29.2	—
Sex																	
Females	8008	47.1	6349	84.4	1157	15.4	0.51	5543	87.3	789	12.4	0.38	3775	68.1	1735	31.3	0.013
Males	8944	52.6	6850	84.2	1262	15.5		5994	87.5	872	12.7		4328	72.2	1618	27.0	
Missing	51	0.3	—	—	—	—		—	—	—	—		—	—	—	—	
Age (mo)																	
<6	6325	37.2	5180	87.5	684	12.1	<0.0001	4566	88.1	603	11.6	0.005	3074	67.3	1479	32.4	<0.0001
6–12	1955	11.5	1563	85.2	254	14.3		1376	88.0	187	12.0		1004	73.0	370	26.9	
12–18	2363	13.9	1842	81.3	429	18.0		1620	87.9	220	11.9		1116	68.9	500	30.9	
18–24	1360	8.0	1079	83.1	221	16.2		954	88.4	124	11.5		677	71.0	275	28.8	
24–36	1547	9.1	1157	80.2	278	18.5		1017	87.9	138	11.9		760	74.7	256	25.1	
36–60	1598	9.4	1113	83.4	243	16.1		933	83.8	180	16.1		713	76.4	220	23.6	
>60	1785	10.5	1255	80.2	313	19.0		1060	84.5	190	15.1		810	76.4	248	23.4	
Missing	68	0.4	—	—	—	—		—	—	—	—		—	—	—	—	
Ward																	
Fee paying	1139	6.7	536	53.4	478	46.4	0.002	331	61.8	205	38.2	<0.0001	222	66.9	94	32.9	0.001
General pediatrics	9385	55.2	7663	87.2	1213	12.6		6772	88.3	826	10.8		4782	70.6	1767	26.1	
Isolation	1071	6.3	815	85.9	203	13.7		677	87.4	103	12.6		447	66.0	198	30.8	
Diarrhea/rehydration	1445	8.5	1260	91.5	125	8.4		1101	89.9	127	10.1		745	67.7	214	22.1	
Malnutrition	3384	19.9	2654	88.4	649	11.5		2396	90.3	257	9.7		1447	60.4	878	36.6	
PICU	544	3.2	310	65.4	158	32.9		281	90.6	28	9.4		222	79.2	50	20.7	
Missing	34	0.2	—	—	—	—		—	—	—	—		—	—	—	—	
Quarter																	
January to March 2006	2229	13.1	1695	79.9	427	20.1	<0.001	1289	76.0	406	24.0	0.001	838	65.0	451	35.0	<0.001
April to June 2006	2505	14.7	1830	76.6	559	23.4		1493	81.5	337	18.5		977	65.4	516	34.6	
July to September 2006	2196	12.9	1921	96.4	71	3.6		1497	77.9	424	22.1		1019	68.1	478	31.9	
October to December 2006	3427	20.2	2621	82.8	543	17.2		2355	89.9	266	10.1		1655	70.3	700	29.7	
January to March 2007	3841	22.6	2938	84.6	533	15.4		2736	93.1	202	6.9		2028	74.1	708	25.9	
April to June 2007	2805	16.5	2234	88.2	298	11.8		2201	87.4	33	12.6		1681	76.4	520	23.6	

PICU, Pediatric Intensive Care Unit.
*Rows totals may be <100%

World Health Organization recently published HIV testing guidelines advocating that in generalized epidemics, HIV testing and counseling be recommended to all patients presenting to a health facility and that HIV testing be incorporated as a routine aspect of care on hospital medical wards and outpatient facilities.[13,37,38] Increased HIV testing has been proposed as an important component of HIV prevention and a pathway to support universal access to

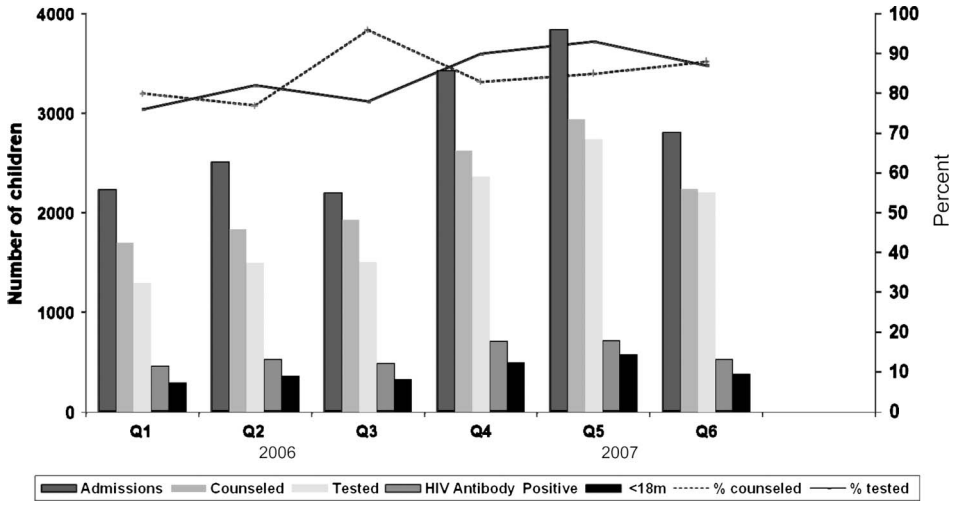

FIGURE 1. Number and percent of children admitted to UTH with unknown HIV status who received HIV counseling and antibody testing by quarter, Lusaka, Zambia, January 2006 to June 2007 (quarter 1 vs. quarter 6, χ^2 test, $P < 0.0001$).

TABLE 2. Children Who Did not Receive HIV Antibody Testing (n = 4099), by Reason not Tested and Counseling Status, UTH, January 2006 to June 2007

			Counseled	
	Total	%	Yes	No
Reason not tested	2111	52.0	716	1395
Child died	920	43.6	88	832
Too sick to approach	36	1.7	10	26
Weekend	101	4.8	5	96
Discharged early	202	9.6	77	125
Transferred to another ward	103	4.9	42	61
Absconded/LAMA	90	4.3	27	63
Waiting for husband's permission	110	5.2	90	20
Not ready	102	4.8	82	20
Parent refused	254	12.0	202	52
Other	193	9.1	93	100
Reason not stated	1988	48.0	952	1036
Total	4099	100	1668	2431

LAMA, left against medical advice.

ART.[39,40] This is particularly important for infants where the rate of disease progression is extremely rapid, the risk of early death is high, and ART can decrease mortality significantly during the first year of life.[14,41]

High acceptance of routine HIV testing and counseling with an option to refuse has been demonstrated in PMTCT programs.[42–45] A recent study in South Africa found that routine outpatient point of care testing resulted in 5 times as many adults newly identified as HIV infected compared with physician referral to an adjacent voluntary counseling site.[46] Similarly, at UTH, testing increased dramatically when it became routinely available on the wards compared with the previous policy of sending children to an adjacent voluntary counseling and testing center.

Financial and human resources for this program were relatively modest. Counselors from an existing service were redeployed to the hospital wards, several volunteer peer counselors were hired, and as the program grew, additional counselors were brought on. Testing kits and phlebotomy supplies were generally available though confirmatory tests were intermittently in short supply. Physicians and nurses were sensitized to the new testing approach, but due to high workload, testing remained in the domain of the counselors.[47] Also, the testing program was only initiated after HIV treatment services were assured.[29] Considerable resources of the Zambian government, the President's Emergency Plan for AIDS Relief program, and other partners currently support the PCOE and the HIV program in district clinics.[28,29] Also, the availability of free ART for children was viewed as an impetus for caregivers to agree to testing their children.

In addition to identifying and making HIV care and treatment services available to more than 3000 HIV-positive children, there were secondary benefits to the program. Parents and caregivers were offered HIV testing and, later in the program, CD4 cell count testing. HIV-positive adults were referred for care. Parents were encouraged to bring their other children to the hospital for evaluation. Another benefit for many families was counseling given to mothers of HIV-exposed infants to enhance safe breastfeeding practices and potentially reduce the risk of HIV postnatal transmission.[48,49]

The establishment of an EID program using DNA PCR represents another significant accomplishment. Two thirds of the HIV-seropositive children were <18 months of age necessitating the availability of diagnostic capacity to distinguish exposed from infected children.[8,50] The proportion of HIV-seropositive children <18 months of age who had a sample sent for DNA PCR ranged from 44% to 76%. Factors preventing all babies from being tested included short hospital stay, high census, limited human resources, and the requirement for venous blood samples. Of note, beyond the first 6 weeks of life, the rate of PCR positivity was greater than 50%, increasing with age to 85% in the 12- to 18-month age group. These rates are considerably higher than those reported in Botswana, where 10% of hospitalized children aged 9 weeks to 9 months and 19% of those aged 9–18 months were DNA PCR positive.[51] Because not all children <18 months of age

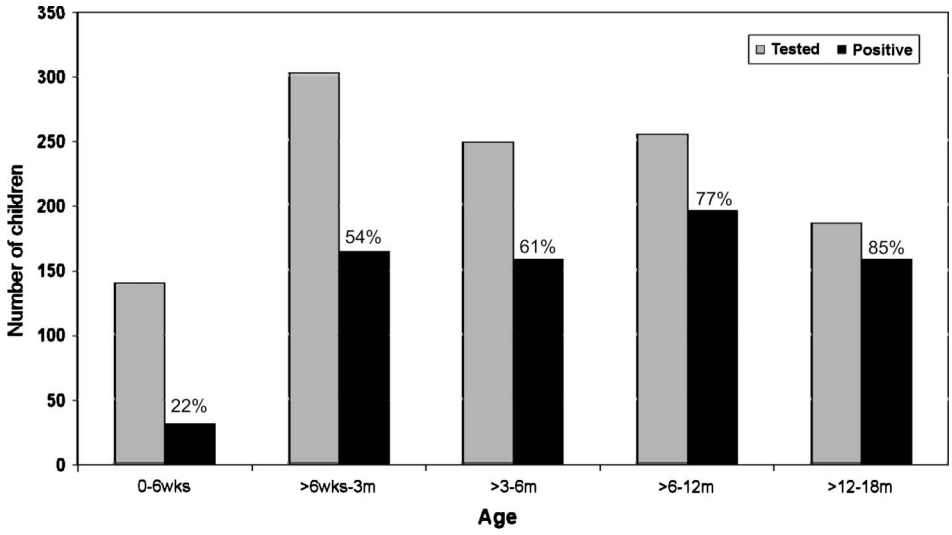

FIGURE 2. DNA PCR positivity rates by age for 1276 HIV-exposed children <18 months of age admitted to the pediatric wards, UTH, Lusaka, Zambia, May 2006 to June 2007.

were tested, we speculate that clinicians selectively tested children with suspicious clinical or laboratory findings. Also UTH is a referral hospital more likely to admit severely ill children compared with district hospitals in the Botswana report. The high rate of PCR positivity at UTH may also speak to the differences in the PMTCT programs: azidothymidine + single-dose nevirapine is the primary regimen in Botswana, whereas the PMTCT program in Lusaka had relied primarily on single-dose nevirapine (efforts are underway to use more efficacious PMTCT regimens in Zambia).[30,42,52] Unfortunately, data were not collected on maternal PMTCT regimens. The high PCR-positive rate speaks to the urgent need to enhance the efficacy of PMTCT regimens and follow-up of HIV-exposed infants.[11,53]

There are several limitations and challenges to the implementation of a routine HIV testing program for hospitalized children. Additional staff and a secure supply chain for commodities such as testing kits and cotrimoxazole were necessary as was training of counselors and hospital staff. It required many months for the new testing approach to be fully accepted by hospital staff many of whom were reluctant to see children tested for concerns that the children were too ill or too young or workload would be increased. Repeated sensitization activities were necessary for staff to accept the benefits of testing children. Also in a high-volume hospital like the UTH, HIV counseling and testing remains within the domain of counseling staff, and testing is generally not done unless counselors are available.

Ensuring follow-up of children identified as HIV seropositive and the return of PCR results to parents posed significant challenges particularly during the initial months. The number of newly identified HIV-positive children outstripped the capacity of the PCOE, and many were not engaged in follow-up care. Similarly, many families did not return to receive PCR results. Systems have since been put in place to enhance linkages between the hospital wards and outpatient clinics and to enhance patient follow-up including a systematic appointment system, assignment of staff to track patient follow-up, improved turnaround for PCR results (now at 4–7 days), documentation of comprehensive demographic data including address and phone information to contact patients who do not attend appointments, and a home visit program with linkages to local community organizations.

In conclusion, we have successfully implemented a routine HIV counseling and testing program for hospitalized pediatric patients at a busy urban hospital in Lusaka, Zambia. More than 3000 HIV-seropositive children were identified and referred for HIV care over 18 months. Furthermore, we initiated an early infant diagnostic testing program using DNA PCR facilitating the diagnosis of HIV infection in the youngest, most vulnerable babies. We propose that this program is particularly relevant in settings with generalized HIV epidemics and should be replicated as a highly feasible way to identify children in need of HIV care and antiretroviral treatment.

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REFERENCES

1. World Health Organization. *Towards Universal Access: Scaling up Priority Interventions in the Health Sector. Progress Report*. Geneva, Switzerland: WHO; June 2008. Available at: http://www.who.int/hiv/pub/towards_universal_access_report_2008.pdf. Accessed March 20, 2009.
2. UNAIDS. *AIDS Epidemic Update December 2007*. Geneva, Switzerland: WHO; November 2007. Available at: http://data.unaids.org/pub/EPISlides/2007/2007_epiupdate_en.pdf. Accessed March 20, 2009.
3. Abrams EJ. Taking stock: triumphs and challenges in the field of pediatric HIV infection. *Therapy.* 2007;4:705–709.
4. Prendergast A, Tudor-Williams G, Jeena P, et al. International perspectives, progress and future challenges of pediatric HIV infection. *Lancet*. 2007;370:68–80.
5. Eley B, Nuttal J. Antiretroviral therapy for children: challenges and opportunities. *Ann Trop Paediatr*. 2007;27:1–10.
6. Kline MW. Perspectives on the pediatric HIV/AIDS pandemic: catalyzing access of children to care and treatment. *Pediatrics*. 2006;117:1388–1393.
7. Committee on Pediatric AIDS, Section on International Child Health. Increasing antiretroviral drug access for children with HIV infection. *Pediatrics*. 2007;119:838–845.
8. World Health Organization. *Antiretroviral Therapy of HIV Infection in Infants and Children in Resource-Limited Settings: Towards Universal Access: Recommendations for a Public Health Approach*. Geneva, Switzerland: WHO; September 2006. Available at: http://www.who.int/hiv/pub/guidelines/pmtctguidelines3.pdf. Accessed March 20, 2009.
9. Ellis JC, L'homme RF, Ewings FM, et al. Nevirapine concentrations in HIV-infected children treated with divided fixed-dose combination antiretroviral tablets in Malawi and Zambia. *Antivir Ther*. 2007;12:253–260.
10. Chokephaibulkit K, Plipat N, Cressey TR, et al. Pharmacokinetics of nevirapine in HIV infected children receiving an adult fixed-dose combination of stavudine, lamivudine and nevirapine. *AIDS*. 2005;19:1495–1499.
11. Stringer E, Chi BH, Namwinga C, et al. Monitoring effectiveness of programs to prevent mother-to-child transmission in lower-income countries. *Bull World Health Organ*. 2008;86:57–62.
12. United Nations Children's Fund. *Children and AIDS. Third Stocktaking Report, 2008*. New York, NY: UNICEF, 2008. Available at: http://www.unicef.org/publications. Accessed March 20, 2009.
13. World Health Organization. *Guidance on Provider-Initiated HIV Testing and Counseling in Health Facilities*. Geneva, Switzerland: WHO, May 2007. Available at: http://whqlibdoc.who.int/publications/2007/9789241595568_eng.pdf. Accessed March 20, 2009.
14. Newell ML, Coovadia H, Cortina-Borja M, et al, and the Ghent International AIDS Society (IAS) Working Group on HIV Infection in Women and Children. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis. *Lancet*. 2004;364:1236–1243.
15. Jones SA, Sherman GG, Coovadia AH. Can clinical algorithms deliver an accurate diagnosis of HIV in infancy? *Bull World Health Organ*. 2005;83:559–560.
16. Horwood C, Liebeschuetz S, Blaauw D, et al. Diagnosis of pediatric HIV infection in a primary health care setting with a clinical algorithm. *Bull World Health Organ*. 2003;81:858–866.
17. Vetter KM, Djomand G, Zadi F, et al. Clinical spectrum of HIV disease in children in a West African city. *Pediatr Infect Dis J*. 1996;15:438–442.
18. Rogerson SR, Gladstone M, Callaghan M, et al. HIV infection among paediatric in-patients in Blantyre, Malawi. *Trans R Soc Trop Med Hyg*. 2004;98:544–552.

19. Reyburn H, Mwakasungula E, Chonya S, et al. Clinical assessment and treatment in paediatric wards in the north-east of the United Republic of Tanzania. *Bull World Health Organ*. 2008;86:132–139.
20. International Center for AIDS Care and Treatment Programs. *Diagnosis of HIV Infection in Infants Using Dried Blood Spots: A Comprehensive Implementation and Clinical Manual*. New York, NY: ICAP, 2007. Available at: http://www.columbia-icap.org/resources/peds/files/Infantdx050307.pdf. Accessed March 20, 2009.
21. Dunn DT, Brandt CD, Krivine A, et al. The sensitivity of HIV-1 DNA PCR in the neonatal period and the relative contributions of intra-uterine and intra-partum transmission. *AIDS*. 1995;9:F7–F11.
22. Ou CY, Yang H, Balinandi S, et al. Identification of HIV-1 infected infants and young children using real-time RT PCR and dried blood spots from Uganda and Cameroon. *J Virol Methods*. 2007;144:109–114.
23. Benjamin DK, Miller WC, Fiscus SA, et al. Rational testing of HIV exposed infant. *Pediatrics*. 2001;108;1–5.
24. Read J, and the Committee on Pedaitric AIDS. Diagnosis of HIV-1 infection in children younger than 18 months in the United States. *Pediatrics*. 2007;120:e1547–e1562.
25. Sherman GG, Jones SA, Coovadia MF, et al. PMTCT from research to reality—results of a routine service. *S Afr Med J*. 2004;94:289–292.
26. Marinda E, Humphrey JH, Iliff PJ, et al. Child mortality according to maternal and infant HIV status in Zimbabwe. *Pediatric Infect Dis J*. 2007; 26:519–526.
27. Mulenga V, Ford D, Walker AS, et al. Effect of cotrimoxazole on causes of death, hospital admissions and antibiotic use in HIV-infected children. *AIDS*. 2007;21:77–84.
28. Stringer JS, Zulu I, Levy J, et al. Rapid scale-up of antiretroviral therapy at primary care sites in Zambia; feasibility and early outcomes. *JAMA*. 2006; 296:782–793.
29. Bolton-Moore C, Mubiana-Mbewe M, Cantrell RA, et al. Clinical outcomes and CD4 cell response in children receiving antiretroviral therapy at primary health care facilities in Zambia. *JAMA*. 2007;298:1888–1899.
30. Stringer JS, Sinkala M, Maclean CC, et al. Effectiveness of a city-wide program to prevent MTCT. *AIDS*. 2005;19:1309–1315.
31. Sherman GG, Stevens G, Jones SA, et al. Dried blood spots improve access to HIV diagnosis and care for infants in low-resource settings. *J Acquir Immune Defic Syndr*. 2005;38:615–617.
32. Stevens W, Sherman G, Downing R, et al. Role of the laboratory in ensuring global access to ARV treatment for HIV-infected children: consensus statement on the performance of laboratory assays for early infant diagnosis. *Open AIDS J*. 2008;2:28–36.
33. DeBaets A, Bulterys M, Abrams EJ, et al. Care and treatment of HIV-infected children in Africa: issues and challenges at the district hospital level. *Pediatr Infect Dis J*. 2007;26:163–173.
34. Kuhn L, Kasonde P, Sinkala M, et al. Does severity of HIV disease in HIV-infected mothers affect mortality and morbidity among their uninfected infants? *Clin Infect Dis*. 2005;41:1654–1661.
35. Marinda E, Humphrey JH, Iliff PH, et al. Child mortality according to maternal and infant HIV status in Zimbabwe. *Pediatr Infect Dis J*. 2007; 26:519–526.
36. Rabie H, de Boer A, Van den Bos S, et al. Children with human immunodeficiency virus infection admitted to a pediatric intensive care unit in South Africa. *J Trop Pediatr*. 2007 [epub ahead of print].
37. De Cock KM, Bunnell R, Mermin J. Unfinished business—expanding HIV testing in developing countries. *N Engl J Med*. 2006;354:440–442.
38. Sanders G, Bayoumi AM, Sundaram V, et al. Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. *N Engl J Med*. 2005;352:570–585.
39. DeCock KM, Marum E, Mbori-Ngacha D. A serostatus-based approach to HIV/AIDS prevention and care in Africa. *Lancet*. 2003;362: 1847–1849.
40. Bunnell R, Mermin J, DeCock KM. HIV prevention for a threatened continent. Implementing positive prevention in Africa. *JAMA*. 2006;296: 855–858.
41. Violari A, Cotton MF, Gibb DM, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med*. 2008;359: 2233–2244.
42. Moses A, Zimba C, Kamanga E, et al. Prevention of mother-to-child transmission: program changes and the effect on uptake of the HIVNET 012 regimen in Malawi. *AIDS*. 2008;22:83–87.
43. Homsy J, Kalamya JN, Obonya J, et al. Routine intrapartum HIV counseling and testing for prevention of mother-to-child transmission of HIV in a rural Ugandan hospital. *J Acquir Immune Defic Syndr*. 2006;42: 149–154.
44. Creek TL, Ntumy R, Seipone K, et al. Successful introduction of routine opt-out HIV testing in antenatal care in Botswana. *J Acquir Immune Defic Syndr*. 2007;45:102–107.
45. Sripipatana T, Spensley A, Miller A, et al. Site-specific interventions to improve prevention of mother-to-child transmission of human immunodeficiency virus. *Am J Obstet Gynecol*. 2007;917:S107–S112.
46. Bassett IV, Giddy J, Nkera J, et al. Routine voluntary HIV testing in Durban, South Africa: the experience from an outpatient department. *J Acquir Immune Defic Syndr*. 2007;46:181–186.
47. Samb B, Celletti F, Holloway J, et al. Rapid expansion of the health workforce in response to the HIV epidemic. *N Engl J Med*. 2007;357: 2510–2514.
48. Iliff PJ, Piwoz EG, Tavengwa NV, et al. Early exclusive breastfeeding reduces the risk of postnatal HIV-1 transmission and increases HIV-free survival. *AIDS*. 2005;19:699–708.
49. Kuhn L, Aldrovandi G, Sinkala M, et al. Effects of early abrupt weaning for HIV-free survival of children in Zambia. *N Engl J Med*. 2008;359: 130–141.
50. Ginsburg AS, Miller A, Wilfert CM. Diagnosis of pediatric human immunodeficiency virus infection in resource-constrained settings. *Pediatr Infect Dis J*. 2006;25:1057–1064.
51. Creek T, Tanuri A, Smith M, et al. Early diagnosis of human immunodeficiency virus in infants using polymerase chain reaction on dried blood spots in Botswana's national program for prevention of mother-to-child transmission. *Pediatr Infect Dis J*. 2008;27:22–26.
52. Chi BH, Chintu N, Lee A, et al. Expanded services for the prevention of mother-to-child HIV transmission: field acceptability of a pilot program in Lusaka, Zambia. *J Acquir Immune Defic Syndr*. 2007:45; 125–127.
53. Abrams EJ, Myers L, Rosenfield A, et al. Prevention of mother-to-child transmission services as a gateway to family-based HIV care and treatment in resource-limited settings: rationale and international experience. *Am J Obstet Gynecol*. 2007;197:S101–S106.